32. (Amended) The method of claim 23, wherein the BDNF is administered at about 10-200 mcg/70 Kg body weight about once every two to six months.

REMARKS

Upon entry of the present Amendment, claims 23-26 and 31-32 will be pending. Claims 28-30 and 33 are canceled without any prejudice and disclaimer and Applicants reserve the rights to pursue the canceled subject matter in a subsequent application. The above-described amendments do not introduce any new matter into the present application.

Election/Restrictions

The Examiner stated that claim 33 is patentably distinct from the invention of Group XIII (1-5, 9, 11-15 and 21) and claim 33 is withdrawn from consideration for being directed to non-elected subject matter.

This objection is overcome by the cancellation of claim 33.

Drawings

The drawings are objected to because of the informalities as indicated by Draftsperson on PTO form 948 (see attached form).

This objection is overcome by the submission of formal drawings herewith (Figures 1-6).

Rejections under 35 U.S.C. § 112

Written description

Claims 23-32 are rejected under 35 U.S.C. 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, the Examiner alleged that the present

specification fails to describe any other "functional derivatives" or fragments of the BDNF that have the same function as BDNF.

This rejection is overcome by the amendment of claim 23.

Enablement

The Examiner acknowledged that the present specification enables a method of treating male erectile dysfunction induced by cavernous nerve damage by administering BDNF to the patient. The Examiner, however, alleged that the specification does not enable any person skilled in the art to which it pertains, to make/use the invention commensurate in scope with these claims. Specifically, the Examiner alleged that:

- The specification does not teach whether BDNF prevent male erectile dysfunction as a result of cavernous nerve damage.
- The specification fails to teach whether BDNF can prevent or treat erectile dysfunction caused by other factors such as arterial insufficiency or venous leakage.
- The specification fails to teach whether administering BDNF to female patients with sexual arousal disorder can provide treatment to those patients.
- The specification fails to teach whether administering BDNF to normal female would prevent future occurrence of sexual arousal disorder.

Applicants respectfully traverse this rejection. In order to make a nonenablement rejection, "the examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention. *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993) (examiner must provide a reasonable explanation as to why the scope of protection provided by a claim is not adequately enabled by the disclosure). A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, unless there is a reason to doubt the

objective truth of the statements contained therein which must be relied on for enabling support." MPEP 2164.04. The Examiner's showing "can be done by making specific findings of fact, supported by the evidence, and then drawing conclusions based on these findings of fact" (emphasis added). *Id.*

However, mere assertion based on personal opinion is not sufficient for showing nonenablement. *See* MPEP 2164.05 ("The examiner should never make the determination based on personal opinion. The determination should always be on the weight of all of the evidence."(emphasis added)). Applicants respectfully request that if the Examiner's rejection is based on facts within his or her personal knowledge, the Examiner will support this rejection with those facts in an affidavit by the Examiner according to MPEP § 2144.03. According to MPEP § 2144.03,

> When a rejection is based on facts within the personal knowledge of the examiner, the data should be stated as specifically as possible, and the facts must be supported, when called for by the applicant, by an affidavit from the examiner.

The present specification teaches that BDNF can be used to treat and prevent various male erectile dysfunction, *e.g.*, erectile dysfunction induced by or secondary to nerve dysfunction, arterial insufficiency, venous leakage, hormonal insufficiency, drug use, surgery, chemotherapy or radiation. *See e.g.*, page 10, lines 3-18 and page 11, lines 12-17 of the present specification. The present specification also teaches that BDNF can be used to treat and prevent various female sexual arousal disorder, *e.g.*, sexual dysfunction induced by or secondary to nerve dysfunction, arterial insufficiency, hormonal insufficiency, drug use, surgery, chemotherapy, or radiation. *Id.* These teachings must be taken as being in compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained in the present specification. It seems that the Examiner based the nonenablement rejection, at least in part, on the Examiner's personal knowledge or opinion. For example, at page 6 of the Office Action, the Examiner stated that:

> Given the complexity of the cause and molecular mechanism of both the erectile dysfunction and female sexual arousal disorder, it is unlikely that one factor is

> responsible for all kinds of erectile dysfunction disorder or arousal disorder. Therefore, targeting only one of the factor is not going to be an effective treatment to such disorders induced by a different factor (emphasis added).

Applicants respectfully request that the Examiner's personal knowledge or opinion be supported, *e.g.*, by an affidavit from the Examiner.

Regarding to the Examiner's allegation that the specification does not teach whether BDNF prevent male erectile dysfunction as a result of cavernous nerve damage, Applicants respectfully submit that the experimental data submitted with Lue 132 Declaration show that BDNF can have preventive, as well as therapeutic, effect to the erectile dysfunction (*See* Lue 132 Declaration at paragraph 5).

Regarding to the Examiner's allegation that the specification fails to teach whether BDNF can prevent or treat erectile dysfunction caused by other factors such as arterial insufficiency or venous leakage, Applicants respectfully submit that the experimental data submitted with Lue 132 Declaration show that BDNF can be used to treat erectile dysfunction not caused or associated with nerve dysfunction, *e.g.*, high fat diet caused erectile dysfunction (*See* Lue 132 Declaration at paragraph 4).

Regarding to the Examiner's allegations that the specification fails to teach whether administering BDNF to female patients with sexual arousal disorder can provide treatment to those patients and the specification fails to teach whether administering BDNF to normal female would prevent future occurrence of sexual arousal disorder, Applicants respectfully submit that the present specification teaches such uses as discussed above. In addition, to expedite prosecution of the present application, Applicants have amended claims to the treatment and prevention of male erectile dysfunction, thus rendering these grounds of rejection moot.

Indefiniteness

Claims 23-32 are rejected under 35 U.S.C. 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, claims 23-32 are rejected under 35 U.S.C. 112,

second paragraph, as allegedly being incomplete for omitting essential steps, such omission amounting to a gap between the steps. The allegedly omitted steps are: How to determine the male erectile dysfunction or female sexual arousal disorder is prevented or treated.

Applicants are somewhat puzzled by this rejection. The presently pending claims are directed to treatment and prevention methods and diagnosing and treatment monitoring steps, although may be desirable, are not necessary for treatment and prevention methods. The undersigned is not aware of any legal authority requiring the inclusion of diagnosing and treatment monitoring steps as part of treatment method claims and respectfully request the Examiner to provide a legal authority for supporting such a requirement. On the other hand, treatment method claims not reciting any diagnosing or treatment monitoring steps are routinely granted. For example, in the U.S. Patent No. 6,436,944, a treatment method claim involving sildenafil (Viagra), as a preferred cGMP PDE elevator, is issued as follows:

> 1. A method of treating impotence comprising co-administering to a patient in need of such treatment an effective amount of:
> (1) a potassium channel opener selected from the group consisting of nicorandil, cromokalim, levcromakalim, lemakalim, pinacidil, diazoxide and minoxidil or a pharmaceutically acceptable salt thereof, and
> (2) a compound which elevates cGMP levels;
> wherein (1) and (2) are each administered orally.

See Exhibit D, Claim 1 of U.S. Patent No. 6,436,944 at column 13, line 65 through column 14, line 6. In addition, diagnostic methods for erectile function are commonly known in the art (*See generally* Exhibit C, Cappelleri).

It is respectfully submitted that the rejections of claims 23-32 under 35 U.S.C. § 112 are overcome by the above remarks and/or amendments and must be withdrawn.

Rejection under 35 U.S.C. § 102

Claims 23, 25, 27 and 31 are rejected under 35 U.S.C. 102(a) as allegedly being anticipated by Bakircioglu *et al.* (2000, *Journal of Urology*, Vol. 163, No. 4 Suppl., pp. 198) (Bakircioglu).

The present application claims priority of a provisional application Serial No. 60/220,031, filed July 21, 2000. Accordingly, the effective U.S. filing date of the present application for 35 U.S.C. § 102(b) analysis is July 21, 2000. MPEP 706.02 and 2133. Since Bakircioglu was published in April. 2000, Bakircioglu is not a 102(b) prior art. Instead, Bakircioglu is a 102(a) prior art. In view of the Declaration of Tom F. Lue pursuant to 37 C.F.R. § 1.132 (*See* Lue 132 Declaration at paragraphs 2-3), the rejection of claims 23, 25, 27 and 31 based on Bakircioglu has been overcome. MPEP 2132.01.

It is respectfully submitted that the rejection of claims 23, 25, 27 and 31 under 35 U.S.C. § 102 is overcome by the above remarks and/or amendments and must be withdrawn.

CONCLUSIONS

Applicants respectfully submit that the rejections of claims 23-32 under 35 U.S.C. §§ 102 and 112 have been overcome by the above remarks and/or amendments. Early allowance of the pending claims 23-26 and 31-32 are earnestly requested.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this

document to **Deposit Account No. 03-1952** referencing 220022001600. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

Date: March 14, 2003 By: _____

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EXHIBIT A

VERSION WITH MARKINGS TO SHOW CHANGES MADE

Please amend claims 23-26, 31 and 32, as follows:

23. (Amended) A method for preventing or treating male erectile dysfunction [or female sexual arousal disorder], which method comprises administering to a mammal to whom such prevention or treatment is needed or desirable, an effective amount of brain-derived neurotrophic factor (BDNF) [or a functional derivative or fragment thereof], thereby preventing or treating said male erectile dysfunction [or female sexual arousal disorder] in said mammal.

24. (Amended) The method of claim 23, wherein the mammal is a human and the BDNF[, or a functional derivative or fragment thereof,] is of human origin.

25. (Amended) The method of claim 23, wherein the BDNF[, or a functional derivative or fragment thereof,] is administered by intracavernous injection, subcutaneous injection, intravenous injection, intramuscular injection, intradermal injection, or topical administration.

26. (Amended) The method of claim 23, wherein the BDNF[, or a functional derivative or fragment thereof,] is administered via a liposome.

31. (Amended) The method of claim 23, wherein the BDNF[, or a functional derivative or fragment thereof,] is administered by intracavernous injection.

32. (Amended) The method of claim 23, wherein the BDNF[, or a functional derivative or fragment thereof,] is administered at about 10-200 mcg/70 Kg body weight about once every two to six months.